

In re application of: SIFFERT, [REDACTED]
Application No.: Not yet assigned
Filed: Herewith
(Continuation of 09/180,783 – Filed: 17 March 1999)

Group:
Examiner:

[REDACTED]
Not yet assigned
Not yet assigned

REMARKS

By the present Preliminary Amendment, Applicants have added the headings suggested by the U.S. Patent and Trademark Office at the appropriate places in the specification. Applicants have amended the claims to better conform them with U.S. practices.

Applicant previously submitted an Amendment to the Sequence Listing in the parent application. In accordance with 37 C.F.R. §§ 1.821 – 1.825, a Substitute Sequence Listing was submitted. Accordingly, Applicant respectfully submits herewith a Transfer Sequence Listing, stating that the content of the paper and computer readable copies of the sequence listing are respectively the same as those in the Substitute Sequence Listing submitted on July 10, 2000 in the parent application.

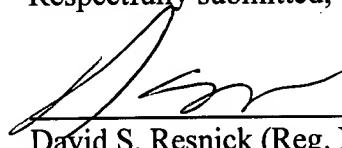
In the event that there are any questions relating to this Amendment or to the application in general, it would be appreciated if the Examiner would contact the undersigned attorney concerning such questions so that prosecution of this application can be expedited.

Entry of the foregoing and prompt and favorable consideration of the subject application on the merits are respectfully requested.

Date: 16 April 2001

Customer No.: 26770

Respectfully submitted,



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VERSION WITH MARKINGS TO SHOW CHANGES MADE TO THE SPECIFICATION

CROSS-REFERENCE TO RELATED APPLICATIONS

This is a continuation of U.S. Patent Application Serial No. 09/180,783 filed on November 16, 1998, the content of which is relied upon and incorporated herein by reference in its entirety, and the benefit of priority under 37 U.S.C. § 120 is hereby claimed.

BACKGROUND OF THE INVENTION:

(i) Field of the Invention

The present invention relates to a method for the diagnosis of diseases by genetic analysis, in particular the analysis of genes for subunits of the human guanine nucleotide-binding proteins (G-proteins).

(ii) Description of the Related Art

Heterotrimeric guanine nucleotide-binding proteins (G proteins) have an outstanding importance in intracellular signal transduction. They mediate the relaying of extracellular signals after stimulation of hormone receptors and other receptors which undergo a conformational change after receptor activation. This leads to activation of G proteins which may subsequently activate or inhibit intracellular effectors (eg. ion channels, enzymes). Heterotrimeric G proteins consist of three subunits, the α , β and γ subunits. To date, several different α subunits, 5 β subunits, and about 12 γ subunits have been detected by biochemical and molecular biological methods (Birnbaumer, L. and Birnbaumer, M. Signal transduction by G proteins: 1994 edition. *J. Recept. Res.* 15:213-252, 1995; Offermanns, S. and Schultz, G. Complex information processing by the transmembrane signaling system involving G proteins. *Naunyn Schmiedebergs Arch.*

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Pharmacol. 350:329-338, 1994; Nürnberg, B., Gudermann, T., and Schultz, G. Receptors and G Proteins as primary components of transmembrane signal transduction. Part 2. G proteins: structure and function. *J. Mol. Med.* 73:123-132, 1995; Neer, E.J. Heterotrimeric G proteins: Organizers of Transmembrane Signals. *Cell* 80:249-257, 1995; Rens-Domiano, S. and Hamm, H.E. Structural and functional relationships of heterotrimeric G-proteins. *FASEB J.* 9:1059-1066, 1995).

SUMMARY OF THE INVENTION:

We have found that a genetic modification in the gene for human G protein β_3 subunits is suitable for the diagnosis of diseases. This genetic modification is particularly suitable for establishing the risk of developing a disorder associated with G protein dysregulation.

BRIEF DESCRIPTION OF THE DRAWING:

The figure depicts a comparison of genes from normotensives and hypertensives by restriction enzyme analysis.

DETAILED DESCRIPTION OF PREFERRED EMBODIMENTS:

The genetic modification which has been found is located in the gene for human G protein $\beta 3$ subunit. This gene has been described by Levine et al. (Proc. Natl. Acad. Sci USA, 87, (1990) 2329-2333). The coding region has an Ser codon (TCC) at position 275, while subjects with an increased risk of disease associated with G protein dysregulation have the codon TCT, which likewise codes for Ser, at this position. The genetic modification is a base substitution at position 825 in which a cytosine (C) is replaced by thymine (T). However, this base exchange is

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“silent” at the amino-acid level, ie. it does not lead to incorporation of a different amino acid at this position. The sequence found in subjects with an increased risk of disease is depicted in SEQ ID NO: 1 in the sequence listing.

ABSTRACT

~~The present invention relates to the use of a genetic modification in the gene for human G protein $\beta 3$ subunit for the diagnosis of diseases.~~

A method of diagnosing a disease comprising determining the presence of a genetic modification in a gene obtained from a subject which encodes a human G protein $\beta 3$ subunit. Also disclosed is a method for establishing the relative risk of developing a disorder associated with G protein dysregulation.